transplant to relapse was 466 days (range 182–729) for the ALL group, and 2270 days (range 130–4410) for the AML/MDS group. The primary cause of death was disease recurrence (n = 11), three ALL and eight AML/MDS patients. Three patients died of acute GVHD, 2 from infection, and for one AML/MDS patient a specific cause of death was not known. These data show that even when relapse after a first HCT occurs, nearly 1/3 of pediatric patients with acute leukemia may still be salvaged with a second HCT.

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EVALUATION OF A POWERED INTRAOSSEOUS DEVICE FOR BONE MARROW SAMPLING

Cohen, S.C., Soroka, J.M. Cancer Care Center of South Texas, San Antonio, TX.

The importance of bone marrow examination in the evaluation of leukemia, multiple myeloma, anemia, pancytopenia, and other disorders is well established. The objective for this study was to evaluate the ability of a powered bone marrow aspiration device to penetrate the intraosseous medullary space of the iliac crest, and to aspirate bone marrow samples for the ultimate purpose of diagnosing disease and monitoring the course of disease and medical therapy. The device was used to obtain bone marrow samples in accordance with accepted practice guidelines and device's directions for use. Among other data, insertion success, time to insertion, and complications were recorded. Patient pain levels were rated from 0 to 10 (10=extreme pain). Device operators rated the use of the device from 0 to 10 (10=outstanding). There were 55 patients in the study from three centers. Successful insertion and aspiration of bone marrow samples were achieved in 54 of the 55 patients (98.1%). Mean insertion time was 4.9 ± 3.0 seconds; significantly faster than the 7.3 minutes reported by Kuball et al* (one-sample *t*-test, $p < 0.001$). There were no complications. The mean insertion pain score was 2.5 ± 2.2 and the mean aspiration pain score was 3.7 ± 2.5. On a scale of 0 to 10, the six operators rated the ease of use of the device at a mean score of 8.3 ± 1.7. Findings suggest that the powered aspiration device is safe and effective for bone marrow aspirations; and that through the use of powered device, needle placement time can be reduced—thereby reducing patient pain.

* Kuball J, Schüz J, Gamm H, Weber M. Bone marrow punctures and pain. *Acute Pain* 2004;6(1):9–14.

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CLOFARABINE PRE-CONDITIONING PRIOR TO ALLOGENEIC STEM CELL TRANSPLANTATION IN HIGH RISK ACUTE MYELOID LEUKAEMIA (AML): A WELL TOLERATED REGIMEN WITH BOTH FULL AND REDUCED TOXICITY SCHEDULES

Richardson, D.S., Hurlock, C., Hill, K., Newman, J., McKeag, N., Groves, L., Orchard, K.H. Southampton University Hospitals, Southampton, Hampshire, United Kingdom.

The outcome for patients with high-risk AML, particularly those with leukaemia at the time of allogeneic transplant remains poor even using full intensity conditioning. A recently published approach used pre-conditioning chemotherapy prior to the delivery of a reduced intensity transplant schedule during the period of cytopenia. Initial results indicate feasibility and potential for long-term disease control.

The bi-halogen purine analogue Clofarabine has significant activity as a single agent in AML and is well tolerated. These characteristics suggest Clofarabine is an ideal agent to use as pre-conditioning therapy.

We have treated 5 patients with high-risk, refractory AML using Clofarabine pre-conditioning to reduce disease burden before full or reduced intensity allogeneic transplantation. In 4 patients, Clofarabine was administered as a single agent (40 mg/m^2/day for 5 days) and in one, in combination with Cytarabine. 2 received reduced toxicity Busulphan-containing transplant schedules; 3 received full intensity, TBI-based conditioning. The indications for using Clofarabine in these patients, included severe allergy to Cytarabine and heavy prior exposure to anthracycline. All 5 patients had marrow involvement with AML prior to administration of Clofarabine. No unexpected toxicity was encountered and the extended period of cytopenia compared with a conventional transplant was manageable in this cohort. One patient who received a reduced intensity regimen, was treated for VOD on the basis of clinical suspicion but liver biopsy showed evidence of grade 3–4 haemosiderosis only. 2 patients who received TBI suffered grade 3–4 mucositis and required parenteral nutrition. All patients achieved >98% donor chimerism at day +30. No patient experienced grade 3–4 acute GvHD. 4 of 5 patients achieved substantial bulk reduction or eradication of marrow AML infiltration following Clofarabine. The patient with Clofarabine-refractory disease achieved CR at day 30 following a full intensity transplant but has relapsed at 4 months post transplant. One patient died in CR at 5 months post transplant from pneumonitis. 3 patients are currently in CR at 2.5–21 months follow up. The use of Clofarabine as a pre-conditioning agent prior to the administration of the transplant conditioning schedule is well tolerated with both full and reduced intensity protocols. This approach to allogeneic transplantation shows promise for the therapy of patients with high risk, refractory AML.

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CLINICAL FEATURES OF ACUTE LEUKEMIA WITH CO-EXPRESSION OF MYELOID AND LYMPHOID ANTIGENS

Jeong, S.H.[1], Lee, H.W.[1], Kang, S.Y.[1], Cho, S.R.[2], Park, J.S.[1], Choi, J.H.[1], Kim, H.C.[1] [1]Ajou University School of Medicine, Suwon, Kyeong-Ki Do, Korea; [2]Ajou University School of Medicine, Suwon, Kyeong-Ki Do, Korea.

Background: Treatment of acute leukemias coexpressing myeloid and lymphoid antigens but does not meet the criteria for biphenotypic acute leukemia by EGIL is uncertain and its prognosis unpredictable. We studied clinical outcomes of those acute leukemia with coexpression. **Method:** Medical charts from 68 patients diagnosed as coexpressing acute leukemia between Jan. 2000 and Dec. 2006 in Ajou University Hospital were reviewed retrospectively. 17/52 AML patients and 5/16 ALL patients received Hematopoietic stem cell transplantation. Significance was obtained by two-tailed Student's *t*-test and survival analyzed by Kaplan-Meier method. **Results:** The median age for all acute leukemia was 42.5 year (15 ~ 83). Age, gender, LDH level and cytogenetics were not different compared to those diagnosed as single lineage acute leukemia at the same time. Forty eight % (16/33) of ALL and 30% (52/176) of AML patients co-expressed counterpart lineage markers. CD19 (11%), CD7 (10%), CD22 (8%), CD5 (8%), CD10 (1%) in AML and CD13 (42%), CD33 (33%), CD14 (3%) in ALL were co-expressed. The co-expressed AML patients showed tendency to short survival duration compared with pure AML patients (18.5 months vs. 24.1 months, $p = 0.069$). Co-expressed AML patients without stem cell transplantation showed shorter survival than pure AML patients (12.9 months vs. 21 months, $p = 0.014$). However in AML who were transplanted, the survival advantage was abrogated (coexpressed vs pure AML; 30 months vs. 35 months, $p = 0.244$). In ALL, survival duration of the co-expressed patients was not shorter than that of pure ALL (19.4 months vs. 21 months) regardless of transplantation. **Conclusion:** AML patients with co-expression of lymphoid markers should be regarded as a poor prognostic group and more aggressive treatment such as transplantation should be considered. Further study on a larger number of patients should be investigated regarding the appropriate criteria for BAL and treatment.

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CENTRAL NERVOUS SYSTEM (CNS) INVOLVEMENT AT DIAGNOSIS DOES NOT ADVERSELY AFFECT THE OUTCOME OF HIGH-DOSE CHEMOTHERAPY AND TRANSPLANT FOR PATIENTS WITH ACUTE MYELOID LEUKEMIA (AML)

Petropoulos, D.[1], Giralt, S.A.[2], Andersson, B.S.[2], Chan, K.W.[3], Rondon, G.[2], Popat, U.R.[2], Hosing, C.[2], Alousi, A.M.[2], Champlin, R.E.[2], de Lima, M.J.[2] [1]MD Anderson Cancer Center,

Houston, TX; [2] MD Anderson Cancer Center, Houston, TX; [3] Texas Transplant Institute, San Antonio, TX.

Objective: To evaluate the impact of the presence of CNS disease at diagnosis in the outcome of AML patients who underwent high-dose chemotherapy and stem cell transplant. **Methods:** We performed a retrospective study of all transplants performed for AML in our institution between 1993 and 2007. Twenty-one patients (11 males) with CNS disease were identified. Five had unclassified AML, 2 M1, 2 M2, 9 M4 and 3 MDS. All but one patient had intermediate or poor cytogenetics. Twelve patients were in remission (4 in CR1, 6 in CR2, 2 in greater CR) at the time of transplant. Four patients had refractory relapse, 4 untreated relapse and one primary induction failure. All patients were in CNS CR at the time of transplant. Median age was 22.5 years (range 2–66). Three patients received autologous graft. The conditioning regimen was chemotherapy-based in 19 patients [Busulfan (Bu)-Fludarabine (Flu): 6; Bu-Cyclophosphamide (Cy)-Thiotepa (TEP): 6; Flu-Melphalan (Mel)-TEP: 2; Flu-Mel: 1; Flu-Mel-Mylotarg: 1; Bu-Cy: 1; Decitabine-Bu-Cy:1; Cy-Etoposide:1]. Two patients received Flu-Mel with TBI. GVHD prophylaxis was tacrolimus-based in 14/18 allogeneic transplants [with methotrexate (MTX) in 13 or steroids in one], cyclosporine-based in 2 (one with MTX, one with steroids) with 2 patients receiving T-cell depleted graft. The donor was matched related in 9, matched unrelated in 4, mismatched related in 4 and mismatched unrelated (cord) in 1. Eleven patients received marrow, 9 PBSC and one cord blood transplant. Patients received intrathecal chemotherapy monthly × 6 months post-transplant as CNS prophylaxis. **Results:** Twelve patients died (hemorrhage: 1, sepsis: 2, acute GVHD: 2, MOF:1, chronic GVHD:1, relapse: 5). With a median follow-up of 7.5 years, 9 patients are alive, 8 in CCR, one in CR after CNS relapse and salvage chemotherapy. **Conclusions:** The presence of CNS disease at diagnosis should not preclude the use of stem cell transplantation as treatment for AML.

LYMPHOMA/MULTIPLE MYELOMA

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QUANTITATIVE MRD MONITORING IDENTIFIES DISTINCT GVL RESPONSE PATTERNS AFTER ALLOGENEIC STEM CELL TRANSPLANTATION FOR CHRONIC LYMPHOCYTIC LEUKEMIA: RESULTS FROM THE GCLLSG CLL3X TRIAL

Dreger, P.[1], Boettcher, S.[2], Stilgenbauer, S.[3], Bunjes, D.[3], Schubert, J.[4], Cohen, S.[5], Hallek, M.[6], Kneba, M.[2], Dohner, H.[3], Ritgen, M.[2] [1] University of Heidelberg; [2] University of Schleswig-Holstein, Kiel; [3] University of Ulm; [4] University of Saarland, Homburg, Germany; [5] Hopital Maisonneuve Rosemont, Montreal, Canada; [6] University of Cologne, Germany.

The purpose of this study was to prospectively analyse minimal residual disease (MRD) kinetics after reduced-intensity allogeneic stem cell transplantation (allo-SCT) in high-risk chronic lymphocytic leukemia (CLL). Subjects were the first 30 consecutive patients from a prospective disease-specific multicenter clinical trial by the German CLL Study Group (study patients), and 7 pilot patients treated identically. All patients had an unfavorable VH mutational status. Donor lymphocyte infusions (DLI) were administered preemptively in case of incomplete chimerism and/or stable or increasing MRD, provided that GVHD was absent after complete withdrawal of immunosuppression.

Results: Using quantitative RQ-PCR and/or flow-based MRD monitoring (sensitivity >=10^{-4}), four distinct patterns of MRD kinetics could be identified: (i) patients who achieved durable MRD negativity without direct evidence of graft-versus-leukemia effects (GVL; n = 4); (ii) patients who showed a complete MRD response to GVL (n = 18); (iii) patients who responded to GVL but failed to reach complete MRD clearance (n = 4); and (iv) patients in whom a GVL effect with subsequent MRD suppression could not be induced (n = 2). Taking into account 2 non-relapse-related deaths, study patients had a 54% probability of being alive and MRD-negative 12 months post transplant. MRD negativity occurring at this time or later was durable in all cases except one. Three-year non-relapse mortality, event-free, and overall survival of study patients was 11%, 58% and 71%, respectively. **Conclusions:** Effective GVL activity can be induced in most patients with high-risk CLL after allo-SCT according to the design chosen here. GVL occurs essentially in the context of chronic graft-versus-host disease induced by immunosuppression tapering or DLI. However, due to development of secondary GVL resistance, in a signficant proportion of cases sustained MRD negativity is not achieved.

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REDUCED INTENSITY VERSUS FULL MYELOABLATIVE STEM CELL TRANSPLANT FOR ADVANCED CHRONIC LYMPHOCYTIC LEUKEMIA

Peres, E., Levine, J., Kato, K., Krijanovski, O., Khaled, Y., Ferrara, J., Yanik, G., Mineishi, S. University of Michigan, Ann Arbor, MI.

Background: Patients with CLL who are refractory to fludarabine have a median survival of 12 months. Reduced intensity conditioning (RIC) for stem cell transplant may decrease transplant related mortality (TRM) compared to full intensity conditioning (FIC), but long term effectiveness is unclear. We compared outcomes of 50 patients with advanced CLL who underwent allogeneic hematopoietic stem cell transplant (HSCT) at the University of Michigan with different intensity conditioning regimens. **Methods:** Twenty one patients with CLL received RIC and 29 received FIC prior to allogeneic HSCT between 1995 and 2005. RIC consisted of Fludarabine (80–125 mg/m^2) Busulfan (6.4 mg/kg IV or 8 mg/kg oral) and Total lymphoid irradiation of 2–4 Gy. FIC consisted of either CVB (cyclophosphamide 1800 mg/m^2, etoposide 200 mg/m^2 and BCNU 450 mg/m^2) (n = 20) or Bu/Cy (busulfan 3.2 mg/kg and cyclophosphamide 60 mg/kg for 2 days) (n = 9). Graft versus host disease prophylaxis consisted of tacrolimus and mycofenolate mofetil in the RIC group and tacrolimus and methotrexate in the FIC group. **Results:** The median age was 56 years (range 41–61 years) in the RIC group and 50 years (range 26–61 years) in the FIC group. There was no difference between groups regarding the number of prior therapies or stem cell source. High risk cytogenetics were present in 50% (11/21) of the RIC group and 68% (20/29) (del 17q13 or del 11q22 or complex cytogenetics) in the FIC group. The donor source consisted of matched unrelated (MUD) 62% (13/29) in the RIC and 45% (9/20) in the FIC group. RIC recipients were significantly more likely to be alive at all times post HSCT (5 y OS RIC 63% versus FIC 18%, p = 0.006). High TRM was the primary cause of inferior survival in the FIC recipients who experienced double the day 100 TRM (FIC 27% versus RIC 14%, p = 0.005). The relapse rate was 14% regardless of conditioning regimen with the majority of relapses occurring after day 100. Likewise the incidence of severe GVHD grade II-IV was similar in both groups (FIC 27% versus RIC 28%). **Conclusion:** These data suggest that RIC results in significant superior overall survival compared to FIC in patients with CLL despite the higher proportion of HLA-disparaty in the RIC group. The lower TRM in the RIC group accounted for the major difference in overall survival.

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UNRELATED CORD BLOOD TRANSPLANTATION IN ADULTS WITH LYMPHOID MALIGNANCIES. A EUROCORD/EBMT-LYMPHOMA WORKING PARTY STUDY

Rodrigues, C.A.[1], Sanz, G.[2], Brunstein, C.[3], Renaud, M.[4], Blaise, D.[5], Rio, B.[6], Cairo, M.S.[7], de Lima, M.[8], Sureda, A.[9], Wagner, J.[3], Gluckman, E.[1], Rocha, V.[1] [1] Eurocord Office, Hopital Saint Louis, Paris, France; [2] Hospital Universitario La Fe, Valencia, Spain; [3] University of Minnesota Medical School, Minneapolis, MN; [4] Hopital La Miletrie, Poitiers, France; [5] Institut Paoli Calmettes, Marseille, France; [6] Hotel Dieu, Paris, France; [7] Columbia University, New York, NY; [8] MD Anderson Cancer Center, Houston, TX; [9] Hospital Santa Creu i Sant Pau, Barcelona, Spain.

Umbilical cord blood transplants (UCBT) from unrelated donors is a feasible option for adults with high-risk acute leukemia. However, little is known about the outcome of UCBT in patients with advanced lymphoid malignancies. We evaluated 104 adult patients (median age, 41 years; range 16–65 years) who received a single